Page 2 of 22

## **AMENDMENT**

The following <u>Listing of the Claims</u> will replace all prior versions and all prior listings of the claims in the present application:

## **Listing of The Claims:**

- 1. (Currently Amended) A method for the selection of a virus <u>bacteriophage</u> comprising the steps of:
- (a) providing a virus comprising a plurality of virions bacteriophage encoding and displaying a fusion polypeptide, said fusion polypeptide comprising a heterologous polypeptide inserted into the sequence of a viral bacteriophage coat protein polypeptide, wherein said plurality of virions bacteriophage comprise a sequence specific protease cleavable site located within the displayed polypeptide and which site is protected by folding of the polypeptide and is otherwise either absent from the bacteriophage, or inaccessible to cleavage, or present only in bacteriophage proteins not required after bacteriophage assembly to mediate infection and wherein cleavage of said sequence specific protease cleavable site impairs infection by a said virion bacteriophage;
- (b) exposing the <u>bacteriophage</u> to a protease that recognizes said <u>sequence specific protease</u> cleavable site, wherein said protease only cleaves said <u>sequence specific protease</u> cleavable site if said fusion polypeptide is not properly folded, such that said exposing selects against <u>virions</u> <u>phage</u> displaying fusion polypeptide that is not properly folded; and
- (c) propagating a virion bacteriophage comprising intact fusion polypeptide.
- 2. (Cancelled)

Page 3 of 22

3. (Currently Amended) The method according to claim 1 wherein after exposing said virus to said sequence specific protease, a virions bacteriophage comprising uncleaved fusion polypeptide is separated from a virion bacteriophage comprising cleaved fusion polypeptide.

4. (Cancelled)

- 5. (Currently Amended) The method according to claim 1, wherein the <u>bacteriophage virus</u> encodes a repertoire of sequences.
- 6. (Previously Presented) The method according to claim 5, wherein the repertoire of sequences encodes the displayed heterologous peptide or protein.
- 7. (Currently Amended) The method according to any one of claims 5 or 6 in which the sequence specific protease cleavable site is comprised within the repertoire of sequences.
- 8. (Cancelled)
- 9. (Currently Amended) The method according to claim 1 in which said virion bacteriophage that is resistant to cleavage displays a folded protein or polypeptide.
- 10. (Currently Amended) The method of claim 9 in which the cleavage site is undertaken under conditions at which some members of the repertoire are at least partially unfolded.
- 11. (Previously Presented) The method of claim 9, wherein the exposing step is undertaken in the presence of a molecule which stabilizes or destabilizes the displayed polypeptide under conditions at which some members of the repertoire are at least partially unfolded.
- 12. (Previously Presented) The method of claim 11, wherein the exposing step is undertaken in the presence of a protein denaturant.

Page 4 of 22

13. (Previously Presented) The method according to claim 1, wherein the exposing step is

undertaken in the presence of a ligand for the heterologous polypeptide.

14. (Previously Presented) The method according to claim 1, wherein the method permits

isolation of a protein or polypeptide with improved stability.

15. (Previously Presented) The method according to claim 5, wherein the repertoire of

sequences encodes a repertoire of displayed proteins which are selected by binding to a ligand.

16. (Cancelled)

17. (Currently Amended) The method according to claim 16 1 in which the coat protein is

that protein encoded by gene 3 of a filamentous bacteriophage.

18. (Previously Presented) The method according to claim 17 in which a cleavage site is

introduced between the second and third domain of the gene 3 protein.

19. (Currently Amended) The method according to claim 16 1 wherein the bacteriophage is

a helper bacteriophage used in conjunction with phagemids.

20. (Previously Presented) The method according to claim 19 in which the encapsidated

nucleic acid of the helper bacteriophage is a phagemid and requires the use of said helper

bacteriophage

21. (Currently Amended) The method according to claim 1, wherein the cleavable site is a

sequence specific protease cleavable site, and the cleaving agent is a sequence specific protease

selected from the group consisting of trypsin, chymotrypsin, thermolysin, subtilisin, GLU-C,

factor XA, Arg-C, and thrombin.

Page 5 of 22

22. (New) The method of claim 1, wherein the sequence specific protease cleavable site is an artificial sequence.

- 23. (New) The method of claim 1, wherein the sequence specific protease cleavable site comprises the sequence of SEQ ID NO: 1.
- 24. (New) The method of claim 23, wherein the sequence specific protease is selected from the group consisting of trypsin, thermolysin, subtilisin, Glu-C, and chymotrypsin.
- 25. (New) The method of claim 1, wherein the heterologous polypeptide is selected from the group consisting of barnase and villin.
- 26. (New) The method of claim 1, wherein the fusion polypeptide further comprises a selectable tag and wherein cleavage removes the tag from the bacteriophage and bacteriophage comprising the tag are selected.